UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trad mark Offic
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

mk

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/874,992	06/12/97	STAMLER J	DUK97-02M

EXAMINER	
CELSA, B	
ART UNIT	**PAPER NUMBER**
1654	9

DATE MAILED: 03/02/99

HM12/0302
HAMILTON BROOK SMITH AND REYNOLDS
TWO MILITIA DRIVE
LEXINGTON MA 02173-4799

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

f.1c

copy

Office Action Summary

Application No.	Applicant(s)
08/874,992	Stamler et al.
Examiner	**Group Art Unit**
Bennett Celsa	1654

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-52* is/are pending in the application.

Of the above, claim(s) *1-14 and 18-48* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *15-17 and 49-52* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

BENNETT CELSA
PATENT EXAMINER

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Claims 1-52 are currently pending.

Claims 1-14 and 18-48 are withdrawn from consideration as being directed to a nonelected invention.

Claims 15-17 and 49-52 are under consideration.

Election/Restriction

1. Applicant's election, without traverse, of Group IV (claims 15-17 and 49-52) in Paper No. 8 is acknowledged. Claims 1-14 and 18-48 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

Information Disclosure Statement

3. The information disclosure statement filed 4/30/98 in paper no. 5 has been considered as indicated by the attached initialed copy of the PTO-1449 Form.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

5. Claims 15-17 and 49-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Stamler et al, WO 93/09806 (5/93).

Stamler et al. disclose the use of a nitrosated hemoglobin (e.g .see definition of "nitrosylation" (page 14, lines 7-11) and specific disclosure of S-nitrosohemoglobin) for promoting vasodilation and platelet inhibition; to treat/prevent cardiovascular disorders (e.g. see page 19, lines 22-25). Cardiovascular disorders include those within the scope of the presently claimed invention (e.g. myocardial infarction, pulmonary embolism, myocardial infarction etc. E.g. See page 18, lines 5-11). The reference teaching of the use of S-nitrosylhemoglobin would immediately envisage (e.g. anticipate) the use of either the oxygenated or deoxygenated forms of hemoglobin e.g. SNO-Hb[FeII]O2 and/or SNO-Hb[FeIII] as presently claimed.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 15-17 and 49-52 are rejected under 35 U.S.C. 103(a) as obvious over Stamler et al, WO 93/09806 (5/93) and Kaesenmeyer, U.S.Pat. No. 5,543,430 (8/96: filed 10/94). .

Stamler et al. generally teach the use of NO donor nitrosylated protein compounds (e.g. especially S-nitrosylated) for use in relaxing smooth muscle and inhibiting platelet aggregation. For example, Stamler et al. disclose the use of a nitrosated hemoglobin (e.g .see definition of "nitrosylation" (page 14, lines 7-11) and specific disclosure of S-nitrosohemoglobin) for promoting vasodilation and platelet inhibition and to treat/prevent cardiovascular disorders (e.g. see page 19, lines 22-25). Cardiovascular disorders include those within the scope of the presently claimed invention (e.g. myocardial infarction, pulmonary embolism, myocardial infarction etc. E.g. See page 18, lines 5-11). The reference teaching of the use of S-nitrosylhemoglobin would immediately envisage (e.g. anticipate) the use of either the oxygenated or deoxygenated forms of hemoglobin e.g. SNO-Hb[FeII]O2 and/or SNO-Hb[FeIII] as presently claimed. The Stamler reference differs from the presently claimed invention which additionally encompasses the use of nitrated hemoglobin as the NO donor.

However, the use of oxidized forms of NO (e.g. nitrites/nitrates) as functionally equivalent NO donors is conventionally known in the art (E.g. See Kaesenmeyer at col. 6). Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize Nitrated/Nitrated hemoglobins in lieu of nitrosohemoglobins in the methods as disclosed by Stamler with a reasonable expectation of success due to functional equivalency of nitrites/nitrates as NO donating compounds.

8. Claims 15-17 and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler et al, WO 93/09806 (5/93) and Hsia, U.S. Pat. No. 5,591,710 (1/97: filed 8/94 or earlier).

Stamler et al. disclose the use of a nitrosated hemoglobin (e.g. see definition of "nitrosylation" (page 14, lines 7-11) and specific disclosure of S-nitrosohemoglobin) for promoting vasodilation and platelet inhibition and to treat/prevent cardiovascular disorders (e.g. see page 19, lines 22-25). Cardiovascular disorders include those within the scope of the presently claimed invention (e.g. myocardial infarction, pulmonary embolism, myocardial infarction etc. E.g. See page 18, lines 5-11). The reference teaching of the use of S-nitrosylhemoglobin would immediately envisage (e.g. anticipate) the use of either the oxygenated or deoxygenated forms of hemoglobin e.g. SNO-Hb[FeII]O2 and/or SNO-Hb[FeIII] as presently claimed. The Stamler reference teaching differs from the presently claimed invention only to the extent that the presently claimed invention encompasses the use of nitrosylated hemoglobins formulated differently than that of Stamler which uses SNOAc as the NO donating entity.

However, as disclosed by the Hsia reference, "A variety of techniques have been described to covalently attach a nitroxide to biomolecules, including hemoglobin ..." (E.g. See Hsia at col. 6, lines 12-36 and recited reference techniques). Additionally, the Hsia reference discloses the indirect covalent attachment of NO to hemoglobin using physiologically compatible macromolecules (e.g. See Abstract and col. 9-26). Accordingly, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to utilize the Hsi reference methods for formulating directly or indirectly attached nitrosylated hemoglobin compounds for

use in the Stamler et al. methods of treating/preventing disease states since Stamler discloses that NO donor compounds, in any form, would be reasonably expected to be useful in their disclosed methods.

Double Patenting

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

10. Claims 15-17 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 30-32 of copending Application No. 08/796,164. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 49-52 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10-15 and 30-32 of copending Application No. 08/796,164. Although the conflicting claims are not identical, they are not patentably distinct from each other because the '164 application discloses the use of S-nitrosylated hemoglobins generally (e.g. claims 30-32) in the presently claimed invention and additionally discloses the making and formulation of a specific S-nitrosylated hemoglobin e.g. SNO-Hb[FeII]O2. Accordingly the selection of the specific S-nitrosylated hemoglobin e.g. SNO-Hb[FeII]O2 and its reduced obvious variant e.g. SNO-Hb[FeIII] for use in the '164 claim 30-32 methods would have been obvious to one of ordinary skill at the time of applicant's invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (703)308-0254.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa

BC

February 23, 1999 BENNETT CELSA PRIMARY EXAMINER